Common Kinetic Scenarios

CHEMISTRY 2310: ADVANCED ORGANIC CHEMISTRY 1
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First order kinetics

- Elementary unimolecular process $\mathbf{A} \xrightarrow{k} \mathbf{P}$ follows first order kinetics

- Differential rate law: $r = \frac{d[\mathbf{P}]}{dt} = -\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}]$

- Integrated rate law: Rewrite differential rate law as $\frac{-d[\mathbf{A}]}{[\mathbf{A}]} = k\,dt$. Then, using the conditions $[\mathbf{A}](0) = [\mathbf{A}]_0$ and $[\mathbf{A}](t) = [\mathbf{A}]$,

$$-\frac{d[\mathbf{A}]}{[\mathbf{A}]} = k\,dt \implies -\int_{[\mathbf{A}]_0}^{[\mathbf{A}]} \frac{d\widetilde{[\mathbf{A}]}}{\widetilde{[\mathbf{A}]}} = \int_0^t k\,d\tilde{t}$$

$$\implies -\left[\ln\widetilde{[\mathbf{A}]}\right]_{[\mathbf{A}]_0}^{[\mathbf{A}]} = \left[k\tilde{t}\right]_0^t$$

$$\implies -(\ln[\mathbf{A}] - \ln[\mathbf{A}]_0) = kt - 0$$

$$\implies [\mathbf{A}] = [\mathbf{A}]_0 e^{-kt}.$$

- Half-life: By definition, $\frac{1}{2}[\mathbf{A}]_0 = [\mathbf{A}]_0 e^{-kt_{1/2}}$, so

$$t_{1/2} = \frac{\ln 2}{k} \approx \frac{0.693}{k}$$

First order kinetics is characterized by a reaction half-life independent of initial concentration $[\mathbf{A}]_0$

- Using $[\mathbf{A}]_0 = [\mathbf{A}] + [\mathbf{P}]$, and $[\mathbf{P}](0) = 0$, $[\mathbf{P}](t) = [\mathbf{P}]$, can also write

$$\frac{d[\mathbf{P}]}{dt} = k[\mathbf{A}] = k([\mathbf{A}]_0 - [\mathbf{P}]) \implies \ln\left(\frac{[\mathbf{A}]_0}{[\mathbf{A}]_0 - [\mathbf{P}]}\right) = kt,$$

a useful form for plotting data

Zeroth order kinetics

- No true zeroth order reactions, reactions only appear this way due to conditions of the measurement, in other words, *pseudo-zeroth order*

- Differential rate law: $r = -\frac{d[\mathbf{A}]}{dt} = k$

- Integrated rate law: $[\mathbf{A}] = [\mathbf{A}]_0 - kt$

- Half-life: $t_{1/2} = \frac{1}{2k}[\mathbf{A}]_0$

Second order kinetics

- Elementary bimolecular process $\mathbf{A} + \mathbf{B} \xrightarrow{k} \mathbf{P}$ follows second order kinetics

- Differential rate law: $r = \frac{d[\mathbf{P}]}{dt} = k[\mathbf{A}][\mathbf{B}]$

Case I: $[\mathbf{A}]_0 = [\mathbf{B}]_0$ or $\mathbf{A} = \mathbf{B}$

• *Convention:* For the case $\mathbf{A} = \mathbf{B}$ (i.e. $2\mathbf{A} \xrightarrow{k} \mathbf{P}$), rate constant k is often redefined such that $-\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}]^2$ holds for easier comparison with the case where $\mathbf{A}$ and $\mathbf{B}$ are different. (Normally, the reaction stoichiometry gives $-\frac{1}{2}\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}]^2$.)

• Integrated rate law: Since $[\mathbf{A}]_0 = [\mathbf{B}]_0$, at any given time, we have

$$[\mathbf{A}] = [\mathbf{A}]_0 - [\mathbf{P}] = [\mathbf{B}]_0 - [\mathbf{P}] = [\mathbf{B}] \implies \frac{d[\mathbf{P}]}{dt} = -\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}][\mathbf{B}] = k[\mathbf{A}]^2.$$

After rearranging,

$$-\frac{d[\mathbf{A}]}{[\mathbf{A}]^2} = k\,dt \implies -\int_{[\mathbf{A}]_0}^{[\mathbf{A}]} \frac{d\widetilde{[\mathbf{A}]}}{\widetilde{[\mathbf{A}]}^2} = \int_0^t k\,d\tilde{t}$$

$$\implies \frac{1}{[\mathbf{A}]} = \frac{1}{[\mathbf{A}]_0} + kt.$$

• Half-life: $\frac{1}{\frac{1}{2}[\mathbf{A}]_0} = \frac{1}{[\mathbf{A}]_0} + kt_{1/2} \implies t_{1/2} = \frac{1}{k[\mathbf{A}]_0}$.

Case II: $[\mathbf{A}]_0 \neq [\mathbf{B}]_0$

• Integrated rate law obtained by rewriting everything in terms of $[\mathbf{P}]$ ($\frac{d[\mathbf{P}]}{dt} = k([\mathbf{A}]_0 - [\mathbf{P}])([\mathbf{B}]_0 - [\mathbf{P}])$), integrating by partial fractions, and reapplying $[\mathbf{A}] = [\mathbf{A}]_0 - [\mathbf{P}]$ and $[\mathbf{B}] = [\mathbf{B}]_0 - [\mathbf{P}]$:

$$\ln\left(\frac{[\mathbf{B}][\mathbf{A}]_0}{[\mathbf{A}][\mathbf{B}]_0}\right) = ([\mathbf{B}]_0 - [\mathbf{A}]_0)kt$$

Pseudo-first order kinetics

• For $\mathbf{A} + \mathbf{B} \xrightarrow{k} \mathbf{P}$, if $[\mathbf{B}] \approx [\mathbf{B}]_0$ throughout the reaction, then $-\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}][\mathbf{B}] \approx k[\mathbf{A}][\mathbf{B}]_0 = k_{\text{obs}}[\mathbf{A}]$, where $k_{\text{obs}} = k[\mathbf{B}]_0$.

• Reasonable assumption to make if $[\mathbf{B}]_0 \gg [\mathbf{A}]_0$ (at least an order of magnitude), or if $\mathbf{B}$ is constantly regenerated (i.e., it's catalytic)

Initial rate kinetics

• At low conversion (typically 5-10%), $[\mathbf{A}] \approx [\mathbf{A}]_0$. If the rate law is $r = -\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}]^n$, then $r = k[\mathbf{A}]_0^n$.
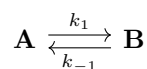
• Can determine order in $\mathbf{A}$ this way: suppose initial rates are measured at two initial concentrations: say, $[\mathbf{A}]_0$ and $[\mathbf{A}]_0' = 2[\mathbf{A}]_0$, and initial rates measured for initial concentrations $[\mathbf{A}]_0$ and $[\mathbf{A}]_0'$ are r and $r' = 8r$, respectively. Then

$$r'/r = 8r/r = 8 = \frac{k[\mathbf{A}]_0'^n}{k[\mathbf{A}]_0^n} = \left(\frac{[\mathbf{A}]_0'}{[\mathbf{A}]_0}\right)^n = 2^n \implies n = 3.$$

Hence, reaction is third order in $\mathbf{A}$.

Equilibrium kinetics

Consider an equilibrium

$$\mathbf{A} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathbf{B}$$

- Let $x = [\mathbf{A}]_0 - [\mathbf{A}]$. Differential rate law: $\frac{dx}{dt} = k_1([\mathbf{A}]_0 - x) - k_{-1}([\mathbf{B}]_0 + x)$

- Integrated rate law:

$$\ln\left(\frac{k_1[\mathbf{A}]_0 - k_{-1}[\mathbf{B}]_0}{k_1[\mathbf{A}]_0 - k_{-1}[\mathbf{B}]_0 - (k_1 + k_{-1})x}\right) = (k_1 + k_{-1})t$$

- Let $x_{\text{eq}} = [\mathbf{A}]_0 - [\mathbf{A}]_{\text{eq}}$. Applying differential rate law at equilibrium ($dx/dt = 0$) yields $k_1[\mathbf{A}]_0 - k_{-1}[\mathbf{B}]_0 = (k_1 + k_{-1})x_{\text{eq}}$. Substituting into the integrated rate law gives $\ln(x_{\text{eq}}/(x_{\text{eq}} - x)) = (k_1 + k_{-1})t$, or

$$[\mathbf{A}] - [\mathbf{A}]_{\text{eq}} = ([\mathbf{A}]_0 - [\mathbf{A}]_{\text{eq}})e^{-(k_1 + k_{-1})t}.$$

In other words, approach towards equilibrium follows first order kinetics with $k_{\text{obs}} = k_1 + k_{-1}$.

Multistep reactions and steady state approximation

In general, no closed form expressions exist, even for the differential rate law, but pre-equilibrium assumption or steady state approximation often give reasonable approximations. Consider a reaction with a reversible first step and irreversible second step:

$$\mathbf{A} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{I} \overset{k_2}{\longrightarrow} \mathbf{B}$$
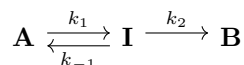
Pre-equilibrium

- Suppose $k_{-1} \gg k_2$. Since conversion to $\mathbf{B}$ is much slower than reversible intercoversion of $\mathbf{A}$ and $\mathbf{I}$, can assume $\mathbf{A}$, $\mathbf{I}$ in equilibrium, with $K = \frac{k_1}{k_{-1}}$:

$$\mathbf{A} \overset{K}{\rightleftharpoons} \mathbf{I} \overset{k_2}{\longrightarrow} \mathbf{B}$$
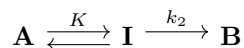
- Differential rate law: using $K = [\mathbf{I}]/[\mathbf{A}]$,

$$r = \frac{d[\mathbf{B}]}{dt} = k_2[\mathbf{I}] = k_2 K[\mathbf{A}] = \frac{k_2 k_1}{k_{-1}}[\mathbf{A}]$$

Steady state approximation (SSA)

- Since $\mathbf{I}$ is a reactive intermediate, $[\mathbf{I}]$ is small and more-or-less constant (steady state) for much of the reaction. Thus, we make the approximation

$$\frac{d[\mathbf{I}]}{dt} = 0 \quad (SSA).$$

- Steady state rate law for example above:
Apply SSA to $\mathbf{I}$:

$$\frac{d[\mathbf{I}]}{dt} = k_1[\mathbf{A}] - k_{-1}[\mathbf{I}] - k_2[\mathbf{I}] = 0$$

Solve for $[\mathbf{I}]$:

$$[\mathbf{I}] = \frac{k_1[\mathbf{A}]}{k_{-1} + k_2},$$

from which

$$r = \frac{d[\mathbf{B}]}{dt} = k_2[\mathbf{I}] = \frac{k_2 k_1}{k_{-1} + k_2}[\mathbf{A}].$$

- Two limiting cases: if $k_{-1} \gg k_2$, then

$$r = \frac{k_2 k_1}{k_{-1} + k_2}[\mathbf{A}] \approx \frac{k_2 k_1}{k_{-1}}[\mathbf{A}],$$
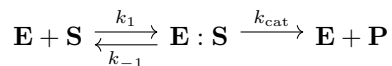
which we derived in the pre-equilibrium case.
On the other hand, if $k_{-1} \ll k_2$, then

$$r = \frac{k_2 k_1}{k_{-1} + k_2}[\mathbf{A}] \approx \frac{k_2 k_1}{k_2}[\mathbf{A}] = k_1[\mathbf{A}].$$

Here, the first step becomes the rate-limiting step, and k_{-1}, k_2 are kinetically invisible.

Michaelis-Menten Kinetics

Consider an enzyme catalyzed reaction with reversible first step and irreversible second step:

$$\mathbf{E} + \mathbf{S} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathbf{E} : \mathbf{S} \xrightarrow{k_{\text{cat}}} \mathbf{E} + \mathbf{P}$$

- Apply SSA to $\mathbf{E} : \mathbf{S}$:

$$\begin{aligned}
\frac{d[\mathbf{E} : \mathbf{S}]}{dt} &= k_1[\mathbf{E}][\mathbf{S}] - k_{-1}[\mathbf{E} : \mathbf{S}] - k_{\text{cat}}[\mathbf{E} : \mathbf{S}] \\
&= k_1([\mathbf{E}]_0 - [\mathbf{E} : \mathbf{S}])[\mathbf{S}] - k_{-1}[\mathbf{E} : \mathbf{S}] - k_{\text{cat}}[\mathbf{E} : \mathbf{S}] = 0
\end{aligned}$$

Solve for $[\mathbf{E} : \mathbf{S}]$:

$$[\mathbf{E} : \mathbf{S}] = \frac{k_1[\mathbf{E}]_0[\mathbf{S}]}{k_{-1} + k_{\text{cat}} + k_1[\mathbf{S}]}$$

Thus,

$$\begin{aligned}
\frac{d[\mathbf{P}]}{dt} = k_{\text{cat}}[\mathbf{E} : \mathbf{S}] &= \frac{k_{\text{cat}} k_1[\mathbf{E}]_0[\mathbf{S}]}{k_{-1} + k_{\text{cat}} + k_1[\mathbf{S}]} \\
&= \frac{k_{\text{cat}}[\mathbf{E}]_0[\mathbf{S}]}{\frac{k_{-1} + k_{\text{cat}}}{k_1} + [\mathbf{S}]} \\
&= \frac{k_{\text{cat}}[\mathbf{E}]_0[\mathbf{S}]}{K_M + [\mathbf{S}]},
\end{aligned}$$

where $K_M := (k_{-1} + k_{\text{cat}})/k_1$ is the *Michaelis-Menten constant*.

- Limiting cases: if $[\mathbf{S}] \gg K_M$, then

$$r \approx \frac{k_{\text{cat}}[\mathbf{E}]_0[\mathbf{S}]}{[\mathbf{S}]} = k_{\text{cat}}[\mathbf{E}]_0 =: V_{\max},$$

so zeroth order (*saturation kinetics*); if $K_M \gg [\mathbf{S}]$, then

$$r \approx \frac{k_{\text{cat}}[\mathbf{E}]_0[\mathbf{S}]}{K_M},$$

so first order in $\mathbf{S}$. When $K_M = [\mathbf{S}]$, then

$$r = \frac{1}{2}V_{\max}.$$

- *Lineweaver-Burk* (double reciprocal) plot: Taking the reciprocal of $r = \frac{V_{\max}[\mathbf{S}]}{K_M + [\mathbf{S}]}$, we obtain

$$\frac{1}{r} = \frac{K_M}{V_{\max}}\frac{1}{[\mathbf{S}]} + \frac{1}{V_{\max}},$$

making it useful to plot $1/r$ (*y*-axis) against $1/[\mathbf{S}]$ (*x*-axis).